

(19) World Intellectual Property
Organization
International Bureau



(43) International Publication Date
15 January 2004 (15.01.2004)

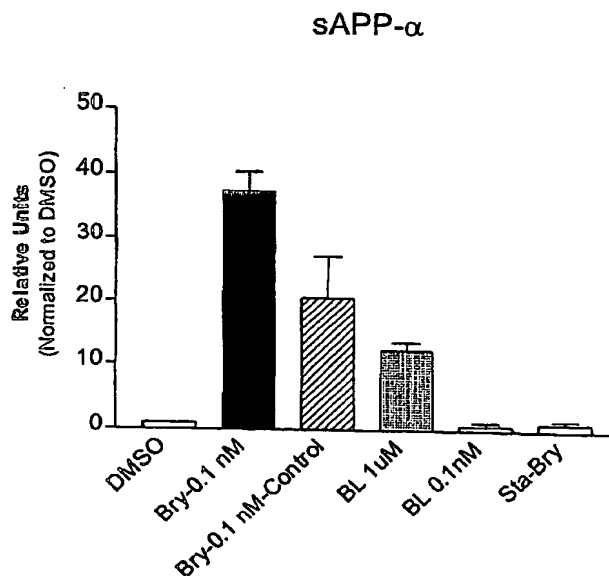
PCT

(10) International Publication Number
WO 2004/004641 A2

- (51) International Patent Classification?: **A61K**
- (21) International Application Number:
PCT/US2003/020820
- (22) International Filing Date: 2 July 2003 (02.07.2003)
- (25) Filing Language: English
- (26) Publication Language: English
- (30) Priority Data:
60/392,951 2 July 2002 (02.07.2002) US
PCT/US03/07101 7 March 2003 (07.03.2003) US
- (71) Applicant (for all designated States except US):
BLANCHETTE ROCKEFELLER NEURO-SCIENCES INSTITUTE [US/US]; 9601 Medical Center Drive, 3rd Floor, Rockville, MD 20850 (US).
- (72) Inventors; and
- (75) Inventors/Applicants (for US only): **ETCHEBER-RIGARAY, Rene** [US/US]; 7604 Westlake Terrace, Bethesda, MD 20817 (US). **ALKON, Daniel, L.** [US/US]; 6701 Bonaventure Court, Bethesda, MD 20817 (US).
- (74) Agent: **STOLE, Einar Ph.D.**; Milbank, Tweed, Hadley & McCloy LLP, 1825 Eye Street, NW Suite 1100, Washington, DC 20006 (US).
- (81) Designated States (*national*): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.
- (84) Designated States (*regional*): ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).
- Published:
— without international search report and to be republished upon receipt of that report

[Continued on next page]

(54) Title: PKC ACTIVATION AS A MEANS FOR ENHANCING sAPP α SECRETION AND IMPROVING COGNITION USING BRYOSTATIN TYPE COMPOUNDS



(57) Abstract: The present invention relates to compositions and methods to modulate α -secretase and/or to improve cognitive ability. The invention further relates the improved/enhanced cognitive ability in diseased individuals, particularly Alzheimer's Disease patients, and treatment thereof through increased sAPP production. Macrocyclic lactones (i.e. bryostatin class and neristatin class) are compounds preferred for use with the present composition. The present invention also provides methods for increasing the generation of non-amyloidogenic soluble APP comprising the activation of protein kinase C (PKC) by administering an effective amount of PKC activator(s).

WO 2004/004641 A2



For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.